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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
BO 42317		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/NL99/00743	03/12/1999	04/12/1998
International Patent Classification (IPC) or national classification and IPC C12Q1/68		
Applicant KEYGENE N.V. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 9 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
VI	☒	Certain documents cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19/06/2000	06.02.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Barz, W Telephone No. +49 89 2399 7320

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/NL99/00743

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-55 as originally filed

Claims, No.:

1-30 as originally filed

Drawings, sheets:

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 30 (IA).

because:

☒ the said international application, or the said claims Nos. 30 (IA) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-16, 18, 23-28

	No:	Claims	17, 19-22, 29-30
Inventive step (IS)	Yes:	Claims	6-13, 15-16, 18, 25-28
	No:	Claims	1-5, 14, 17, 19-24, 29-30
Industrial applicability (IA)	Yes:	Claims	1-29
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

ITEM III:

Claim 30 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(v) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

ITEM V:

Reference is made to the following document:

D1: WO 97 27317 A (AFFYMETRIX INC.), 31 July 1997; cited in the application.

1. NOVELTY

Claims 17, 19-22, and 29-30 do not meet the requirements of Article 33(2) PCT for the following reasons:

1.1 Document D1 discloses a method for providing an array of nucleic acid sequences bound to a carrier, comprising all the steps of **claim 17** of the present application (page 79, line 3 - page 80, line 25; especially page 80, lines 23-25; figure 14). Therefore, the subject-matter of claim 17 is not novel in the sense of Article 33(2) PCT.

1.2 Similarly, arrays obtainable by the method of claim 17 are known from D1 (figure 14), thereby destroying novelty of **claim 19**.

1.3 Methods for analysing nucleic acid sequences, comprising hybridising said nucleic acids with an array of present claim 19, are also disclosed in D1 (page 80, lines 23-25; figure 14). Therefore, the subject-matter of **claims 20-22** is not novel in the sense of Article 33(2) PCT. It is drawn to the applicant's attention the expression "more specifically [...]" in claim 21 has no limiting effect, but is regarded as entirely optional (PCT Guidelines III-4.6).

1.4 The kits of parts comprising an array according to claim 19 is also known from D1 (claims 39-41), thereby destroying novelty of **claim 29**.

1.5 Finally, results or data obtainable by analysing a mixture of nucleic acids with an array according to claim 19 or by a method according to any of claims 20-22 are also disclosed throughout D1, thereby anticipating the subject-matter of **claim 30**.

2. INVENTIVE STEP

2.1 Document D1, which is considered to represent the closest prior art, discloses an array for analysing nucleic acid sequences comprising a carrier carrying at least two different DNA restriction fragments (page 80, lines 1-25; figure 14). Compared to D1, the subject-matter of **claim 1** differs only in that the nucleic acid sequences bound to the carrier correspond to restriction fragments obtainable by using at least one frequent cutter and at least one rare cutter restriction enzyme. The effect of said difference (i.e. the choice of one frequent cutter and one rare cutter) is the reduction of the size of the restriction fragments while, at the same time, targeting rare sequences (see page 13, lines 6-11, of the present application). The technical problem to be solved by the claim 1 may therefore be regarded as how to provide a array carrying nucleic acid fragments having a preferred size. However, in DNA fingerprinting, the choice of restriction enzymes which allow suitable fragments lengths falls within the scope of the customary practice followed by skilled persons, especially as the advantages thus achieved can readily be foreseen (see e.g. D1, page 78, lines 17-25). Therefore, it would be obvious to the skilled person to apply the choice of at least one frequent cutter and at least one rare cutter restriction enzyme to a DNA array according to D1, thereby arriving at an array according to claim 1. Therefore, the subject-matter of **claim 1** does not appear to involve an inventive step (Article 33(3) PCT).

2.2 The dependent **claims 2-5 and 14** do not contain any features which, in combination with the features of claim 1, meet the requirements of the PCT with respect to inventive step, because the additional features of these claims are also known from D1 (page 7, lines 9-14; page 9, lines 3-5 and 10-11; figures 1-5 and 15).

2.3 Compared to D1 (page 80, lines 23-25; figure 14), the method of present **claim 23** differs only in that the nucleic acids to be analysed comprise a mixture of restriction fragments obtained by using one frequent cutter and one rare cutter restriction enzyme. However, this difference cannot be considered inventive for the reasons outlined in item 2.1 above.

2.4 Similarly, the method of **claim 24** cannot be regarded as involving an inventive step, because the amplification of the target DNA prior to hybridisation with the array is also known from D1 (page 9, lines 21-25; page 81, figure 15).

2.5 In contrast, **claim 6** appears to involve an inventive step (Article 33(3) PCT) for the following reason: Compared to D1, the subject-matter of claim 6 differs by (i) carrier-bound sequences corresponding to restriction fragments obtainable by using at least one frequent cutter and at least one rare cutter restriction enzyme (see item 2.1 above) and (ii) said restriction fragments corresponding to AFLP-markers. While the first difference appears to be obvious to the skilled person (see above), the attachment of AFLP-markers to an array is neither disclosed nor suggested by the available prior art. Therefore, the skilled person would have no incentive to attachment such AFLP-markers to the carrier according to D1, thereby arriving at the subject-matter according to claim 6. Consequently, the subject-matter of claim 6 appears to involve an inventive step.

2.6 **Claims 7-12** are dependent on claim 6 and as such also meet the requirements of the PCT with respect to inventive step.

2.7 **Claim 13** seems to involve an inventive step for analogous reasons.

2.8 Similarly, the methods of **claims 15-16 and 18** appear to involve an inventive step for analogous reasons as outlined in item 2.5 above.

2.9 The method of **claim 25** seems to be inventive, because the available prior art does not appear to provide the skilled person with any hint to amplify the restriction fragments by AFLP.

2.10 Finally, the methods of **claims 26-28** also appears to be inventive.

3. INDUSTRIAL APPLICABILITY

The subject-matter of **claims 1-29** appears to be industrially applicable in the sense of Article 33(4) PCT.

ITEM VI:

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO 99/23256	14.05.99	30.10.98	30.10.97

The above patent document was published after the priority date, but before the filing date of the present application. Therefore, it is only relevant for those parts of the present application which do not have a valid claim to priority. Moreover, the above patent document may become relevant prior art in the Regional phase of the present application.

ITEM VII:

1. The incorporation of disclosures by reference (see passages on page 2, lines 8 and 18, page 3, lines 20-22, page 13, lines 10-11 and 17, page 16, line 30, page 17, line 2, and page 18) is not allowed (PCT Guidelines II-4.17).

2. In contrast to the requirements of PCT Guidelines II-4.18, the description refers to unpublished documents on page 3, line 20, and page 22, line 30.

ITEM VIII:

1. The terms "frequent cutter" and "rare cutter" used in **claims 1 and 23** are vague and unclear and leave the reader in doubt as to the meaning of the exact scope of

these features, thereby rendering the definition of the subject-matter of said claims unclear (Article 6 PCT; PCT Guidelines III-4.5).

2. **Claim 3** is unclear (Article 6 PCT), because the meaning of the expression "and corresponds with" is not apparent.

3. **Claim 13** is unclear (Article 6 PCT), because it relates to the "AFLP-markers" of claims 1-12, although claims 1-5 do not mention any AFLP-marker.

4. Similarly, **claim 24** is not clear, because it relates to "the mixture of restriction fragments" of claims 20-23, although claims 20-22 do not mention any such mixture.

5. Finally, **claim 26** is not clear (Article 6 PCT), because it relates to the AFLP-markers of the method of claims 20-25, although these markers are no essential feature of claims 20-24.